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10/725,843	12/02/2003	Hans Kurt Pingel	6207.520-US	3225

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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
05/02/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/725,843	PINGEL ET AL.	
	Examiner	Art Unit	
	SHERIDAN SWOPE	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *April 4 & 17, 2008* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-15 and 17-24* is/are pending in the application.

4a) Of the above claim(s) *17-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0408*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Request for Continuing Examination of April 4, 2008 and Amendment of April 17, 2007 are acknowledged. It is acknowledged that Claims 1, 9, and 15 have been amended. Claims 1-6, 8-15, and 17-24 are pending. Claims 17-24 were previously withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions. Claims 1-6 and 8-15 are hereby reconsidered.

Priority

Applicants have again requested that the present claims be accorded the benefit of DK PA 2000 01456, filed October 2, 2000. In support of said request, Applicants argue that DK PA 2000 01456, page 12, states: "In a preferred embodiment, the growth medium that is added to the cells contains no protein or other component that was isolated from an animal tissue or an animal cell culture." This argument is not found to be persuasive for the following reasons. It is acknowledged that page 12 of DK PA 2000 01456 makes said statement. However, said statement does not encompass the full scope of Claims 1-6 and 8-15 herein. Claims 1-6 and 8-15 herein recite a method using "medium lacking animal-derived components". The broadest reasonable interpretation of "medium lacking animal-derived components" encompasses medium lacking recombinantly produced components that are naturally expressed in animals. DK PA 2000 0145 fails to disclose a method using medium lacking animal-derived components, wherein the animal-derived components are recombinantly produced components that are naturally expressed in animals. Therefore, the priority date granted for the elected invention is October 2, 2001, the filing date of US 09/969,357, which discloses large-scale production of a Factor VII polypeptide using medium lacking animal-derived components (pg 24).

Information Disclosure Statement-Objections

Objection to the Information Disclosure Statement filed December 2, 2003 is withdrawn.

Claim Rejections - 35 USC § 101

Provisional rejection of Claims 1-6, 8-11, and 15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-3, 5, 8, 10-13, and 15-17 of US Application 10/394,086, for the reasons explained in the prior actions, is maintained.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-6 and 8-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

For Claims 1 and 15, the phrase "large-scale production" renders the claim indefinite. It is unclear whether said phrase means large volume production, large amount production, both large volume and large amount, or some other large parameter. In addition, the term "large" is a relative term which renders the claim indefinite. The term "large" is not defined by the claim and the specification does not provide a standard for ascertaining the requisite degree. Thus, if "large-scale production" means large volume production, the skilled artisan would not be apprised of what volume would be considered to be large: 500ml, 1L, 3L, 10L, or some other volume? Likewise, if "large-scale production" means large amount production, the skilled artisan would be apprised of what amount would be considered to be large: 500mg, 1g, 3gm, 10g, or some other amount? Thus, the skilled artisan would not be apprised of the metes and

bounds of the recited invention. Claims 2-6 and 8-14, as dependent from Claim 1, are indefinite for the same reasons. For purposes of examination, it is assumed that "large-scale production" means large-scale volume production.

For Claims 1 and 15, the phrase "pre-determined density" renders the claim indefinite. Neither the specification nor the claims define what density is the "pre-determined density". The skilled artisan would not be apprised of the metes and bounds of the recited invention. Claims 2-6 and 8-14, as dependent from Claim 1, are indefinite for the same reasons.

For Claims 1 and 15, the phrase "animal derived components" renders the claim indefinite. It is unclear whether said phrase means (i) components isolated from tissues or cells of an animal, (ii) components isolated from established animal cell-lines, and/or (iii) recombinantly produced components that are naturally expressed in animals. The skilled artisan would not be apprised of the metes and bounds of the recited invention. Claims 2-6 and 8-14, as reciting said phrase and/or being dependent from Claim 1, are indefinite for the same reasons. For purposes of examination, it is assumed that "animal derived components" encompasses components isolated from animal tissues or cells and recombinant components that are naturally expressed in animals.

For Claims 1 and 15, the term "bioavailability" renders the claim indefinite. It is acknowledged that the specification states: '"Bioavailability" refers to the proportion of an administered dose of a Factor VII … that can be detected in plasma at predetermined times after administration.' However, neither the specification nor the claims define conditions under which the Factor VII is to be administered, the test animal, or the time at which the "bioavailability" is assessed. The skilled artisan would not be apprised of the metes and bounds of the recited invention. Claims 2-6 and 8-14, as dependent from Claim 1, are indefinite for the same reasons.

For Claims 1 and 15, the phrase "said reference preparation comprises FactorVII produced in the presence of serum" renders the claim indefinite. Neither the specification nor the claims define all conditions under which the "reference preparation" is produced. The skilled artisan would not be apprised of the metes and bounds of the recited invention. Claims 2-6 and 8-14, as dependent from Claim 1, are indefinite for the same reasons.

For Claim 5, the phrase "suspension culture competent" renders the claim indefinite. It is unclear whether said phrase encompasses cultures in which the cells are grown free-floating in suspension and/or cultures in which the cells are grown on microcarriers that are free-floating in suspension. The skilled artisan would not be apprised of the metes and bounds of the recited invention. For purposes of examination, it is assumed that the phrase "suspension culture competent" encompasses cultures in which the cells are grown free-floating in suspension as well as cultures in which the cells are grown on microcarriers that are free-floating in suspension.

Claim 10 is rejected under 35 USC 112, second paragraph for improper antecedent basis. It is suggested that for Claim 8, the phrase "macroporous culture" be amended to "macroporous cell culture".

For Claim 11, the phrase "a pre-determined temperature" renders the claim indefinite. Neither the specification nor the claims define what temperature(s) is the "pre-determined temperature". The skilled artisan would not be apprised of the metes and bounds of the recited invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, 6, 8-11, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Reiter et al, 2000 (IDS). Reiter et al teach a method for large-scale production (col 4, parg 8), using a seed culture of recombinant CHO cells expressing wild-type Factor VII grown in medium devoid of animal-derived components (col 4, parg 6), wherein the large-scale production, optionally, uses microcarriers comprising said recombinant CHO cells (col 5, parg 10; Example 5) and medium devoid of animal-derived components (col 6, parg 5). Reiter et al teach additional limitations of these claims as follows. The Factor VII-expressing cells are suspension competent, the Factor VII-expressing cells have been adapted to growth in medium lacking animal-derived components (Example 1), and/or the maintaining step comprises replacement of medium (Example 5). In addition, it is more likely than not that the glycosylation pattern in CHO cells would be different from the glycosylation pattern in vivo (in any mammal except Chinese hamster) or in BHK cells. Therefore, Claims 1-3, 5, 6, 8-11, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Reiter et al, 2000.

In support of their request that the prior rejections be withdrawn, Applicants provide the following arguments, which are relevant here.

(A) Applicants believe that the present claims are entitled to the priority of DK PA21000 01456, filed October 2, 2000.

(B) Prior to the instant invention, the skilled artisan could have no expectation of success in overcoming the known problems of immunogenicity and stability, as for the recombinant proteins produced by the recited method.

(C) The recited invention requires the Factor VII product to have higher bioavailability than that of a reference preparation.

These arguments are not found to be persuasive for the following reasons.

(A) Reply: For the reasons explained above, under "Priority", the Office does not believe that the instant invention is entitled to the priority of DK PA21000 01456, filed October 2, 2000.

(B) Reply: The instant claims do not recite any functional limitations relevant to the immunogenicity or stability of the recombinant Factor VII produced. Therefore, such limitations are not relevant to the instant claims.

(C) Reply: The Office does not have the facilities to test the bioavailability of any recombinant Factor VII. It is up to Applicants to provide evidence that Factor VII produced using the method of Reiter has functional characteristic that differ from the Factor VII produced with the recited method. Moreover, since the method of Reiter et al is equivalent to the method recited herein, the skilled artisan would believe that, more likely than not, the products produced have the same functional characteristics.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reiter et al, 2000 in view of Chen et al, 1998. The teachings of Reiter et al are described above. Reiter et

al do not specifically teach the seed culture being transferred to a vessel of intermediate volume or cooling of their culture prior to sedimentation. However, Chen et al teaches what was well known in the art; transferring a seed culture to a vessel of intermediate volume (pg 5.10.16) and cooling of mammalian cell cultures prior to sedimentation (pgs 5.10.21). It would have been obvious to a person of ordinary skill in the art to adapt the method of Reiter to incorporate the vessel of intermediate volume and the cooling steps of Chen et al. Motivation to do so derives from the desire to gently bring the cells up to a large volume and to cool the cells to avoid continued metabolism and possible death during processing. The expectation of success is high, as using a vessel of intermediate volume and cooling of mammalian cell cultures prior to sedimentation is well known in the art. Therefore, Claims 4 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reiter et al, 2000 in view of Chen et al, 1998.

Claims 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reiter et al, 2000 in view of Chen et al, 1998. Reiter et al teach pulse feeding of cultures 1-4 times per 24 hours as well as continuous feeding (col 6, parg 2). Reiter et al do not teach feeding the cultures with medium comprising glucose. Chen et al teach what was well known in the art; that cultures of mammalian cells can be fed with medium comprising glucose (pgs 5.10.14 & 5.10.17). It would have been obvious to a person of ordinary skill in the art to adapt the method of Reiter to feed the Factor VII-expressing cells with glucose, as taught by Chen et al. Motivation to do so derives from the fact that glucose can be used as an energy source for cultured mammalian cells. The expectation of success is high, as growth of cultured mammalian cells in medium comprising glucose is well known in the art. Therefore, Claims 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reiter et al, 2000 in view of Chen et al, 1998.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652